Claims

1. Process for instabilizing viral quasi-species-distributions under avoidance of resistance phenomena by replication of the nucleic acids of the viruses present in the quasi-species-distribution by means of a defective replication system,

   a)

   - whereby the defective replication system has a rate of misincorporation for nucleotides higher than the rate of misincorporation of the viral wild-type-replication system and,
   - whereby the viruses are replicated by the replication system having the higher rate of misincorporation at least as effectively as it is done by the replication system of the wild-type virus,

   b)

   and/or negative influence of the replication of the consensus-sequence (nucleic acid sequence of the wild-type virus) in relation to other replicatable nucleic acids.

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2. Process according to claim 1, whereby the defective replication of the viral nucleic acid is induced by reaction of a chemical substance.

3. Process according to claim 1, whereby the chemical substance acts as a antimetabolite or allosteric effector of the replication system.

4. Process according to any one of claims 1 to 3, whereby the defective replication is a variant of a natural mutant spectrum of the quasi-species or a mutant produced by mutagenesis.

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5. Process according to any one of claims 1 to 3, whereby via the infiltration of a viral replication system into the virus population with subsequent infection of the target cells of the virus infection (target cells) or by direct infiltration of a viral replication system or components of a viral replication system into the target cells, the latter are enabled to replicate a infected wild-type virus above the replication error threshold of the viral replication system. i.e., to replicate with higher replication error rate than those of the respective stable quasi-species-distribution, having at least the same efficiency of replication.

6. Process according to any one of claims 1 to 5, whereby the replication systems RNA or DNA are polymerases or cofactors of RNA or DNA polymerases.

7. Process according to any one of claims 1 to 6, whereby the infiltration of the defective replication system into the virus population occurs by transformation of individuals of the respective virus population or of the target cell in a per se known manner of the gene therapy.

8. Process according to any one of claims 1 to 6, whereby the infiltration of the defective replication system occurs by superinfection of the target cell with defective viruses of the same species which carry the defective replication system.

9. Process according to any one of claims 1 to 8, whereby the gene carrying the viral replication system with the higher replication error rate was obtained or was synthetically prepared by clonal selection, and was infiltrated into a virus individual or into a target cell by a per se known genetechnical procedure.

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10. Process according to at least one of the claims 1 to 9, whereby the gene coding for the viral replication system with the higher error rate is provided with further regulatory gene segments which take over further control functions in the transformed virus individual or in the transformed target cell.

11. Process according to claim 10, whereby the further regulatory gene segment takes care for a higher replication rate of the virus population.

12. Process according to claim 1, whereby in the alternative b) the other replicatable nucleic acid is more effectively replicated than the nucleic acid of the consensus-sequence.

13. Process according to one of the claims 1 and/or 12, whereby the characteristic superiority parameter (s) is diminished by a combination of the replication system and one or more nucleases and/or ribozymes and/or antisense-RNA, whereby one or more nucleases and/or ribozymes and/or antisense-RNA are directed to components of the respective virus genome and/or the other replicatable nucleic acid is present in the not infected target cell only in a minor concentration in the form of replicator or replicator precursor, and will be replicated only after the infection by the polymerase of the infected virus.

14. Process for the treatment or prophylaxis of viral diseases, whereby either the affected target cells are transformed with a vector system, particularly a viral vector system, having at least one viral replication system which is leading to a replication system with higher rate of misincorporation, or the target cells are transformed by infiltration of a viral system which is leading to a higher error rate of rate of misincorpora-

tion, or the target cells are treated with one or more substances which cause an increased rate of misincorporation of the replication.

15. Process according to one of the claims 1 to 14, whereby the host cells being the target cells of the viral infection are monocellular organisms or bacteria, plant cells or animal host cells like blood cells or erythropoietic stem cells.

16. Nucleic acid (replicator or replicator precursor) obtainable by reaction of nucleotides and a viral replication system as well as other factors which are necessary for the reproduction of viruses under formation of oligo- or polynucleotides, whereby it is exclusively selectioned towards maximum amplification of the oligo- or polynucleotides by the viral replication system.

17. Nucleic acid according to claim 16, characterized in that the nucleic acid sequence is partly homologous or identical to such sequences which are formed in vitro or intracellularly, if by or by action of the viral replication system it is concurrently directed to the most rapidly replicating variant, without maintaining all or some of the functions which are necessary for the wild-type virus, like protein coding functions or functions which are regulating the expression.

18. Nucleic acid according to claim 16 and/or 17, characterized in that it has at least one of the following properties:

- the replicator has intracellularly a significantly shorter replication time than the naturally viral substrate,

- the binding constant of the replicator to the corresponding polymerase is greater than the one of the natural nucleic acid,

- the replicator has no functional binding site for effectors having negative feedback-effect to the replication,

- is produced from a precursor molecule by nucleolysis, either by the use of nucleolytic enzyme or by the fact that the precursor molecule itself contains a ribozyme structure.

19. Nucleic acid according to one of the claims 16 to 18, characterized in that the replicators and replicator precursors are identical or homologous to the so called defective virus nucleic acids (DI-particles) or satellite-RNA.

20. Agent for the performance of the process according to one of the claims 1 to 15 containing a nucleic acid according to one of the claims 16 to 19 or a nucleic acid coding for a nucleic acid according to one of the claims 16 to 19.

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21. Agent according to claim 20 containing at least one gene segment coding for a viral replication system and/or a co-factor of a viral replication system, whereby the system to be coded is leading to a viral replication system with a higher rate of misincorporation than fixed by the native replication system, whereby the efficiency of the replication is at least maintained.

22. Agent according to claim 20 and/or 21 containing together with the replication system, which is leading to higher rates of misincorporation, transformed viruses, phages or eu- or procaryotic cells and/or respectively prepared

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phages or plasmids for the transformation of the target cell or transformed target cells themselves.

23. Agent according to one of the claims 20 to 22, characterized in that they cause as so called replication enzymes a replication above the inherent error threshold under an at least equal replication efficiency as compared with the wild-type.